

## Claims

1. A nucleic acid construct comprising a nucleic acid sequence comprising a reporter gene encoding a reporter protein that is secretable as a protein or product from a cell where it is expressed or produced and that is excretable from a whole animal.
2. A nucleic acid construct according to claim 1 wherein the secretable/excretable protein or product is produced by modulated gene transcription.
3. A nucleic acid construct according to claim 1 wherein the secretable/excretable protein or product is produced by increased reporter translation.
4. A nucleic acid construct according to claim 3 wherein the increased reporter translation is as a result of increased stability or decreased turnover of mRNA.
5. A nucleic acid construct according to claim 1 wherein the secretable/excretable protein or product is produced by post-translational modulation.
6. A nucleic acid construct according to claim 5 wherein the post-translational modulation is increased reporter stability through removal of polyubiquitination or as the result of accumulation or excretion of small molecule metabolites
7. A nucleic acid construct according to any preceding claim further comprising a peptide tag optionally in the form of an epitope tag.
8. A nucleic acid construct according to any preceding claims additionally comprising a promoter element upstream of the (i) a nucleic acid sequence encoding a secreted/excreted protein, and/or (ii) a nucleic acid sequence encoding a peptide tag.
9. A nucleic acid construct according to any preceding claim wherein the secreted/excreted reporter protein is SEAP.

10. A nucleic acid construct according to claim 9 wherein the construct further includes a CypA1 promoter.
- 5 11. A nucleic acid construct according to any of claims 1 to 8 wherein the secreted/excreted reporter protein is a modified human  $\beta$  choriogonadotrophin (hCG) molecule.
12. A nucleic acid construct according to claim 11 wherein the construct further includes a stratifin gene promoter.
- 10 13. A nucleic acid construct according to either claim 11 or 12 wherein the hCG is tagged.
14. A nucleic acid construct according to claim 13 wherein the hCG is myc-tagged.
- 15 15. A nucleic acid construct according to any of claims 1 to 8 wherein the secreted/excreted reporter protein/product is selected from the group comprising hormonal molecules, antibodies and enzymatic molecules..
- 20 16. A nucleic acid construct according to claim 15 wherein the hormonal molecule is FSH.
17. A nucleic acid construct according to claim 15 wherein the antibody is a  $\gamma$  or light chain (Bence Jones) protein.
- 25 18. A nucleic acid construct according to claim 15 wherein the enzymatic molecule is feline urinary carboxylase.
19. A host cell transfected with at least one nucleic acid construct according to any one of claims 1 to 18.
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20. A cell line transfected with at least one nucleic acid construct according to any one of claims 1 to 18.
21. A transgenic non-human animal in which the cells of the non-human animal express the protein encoded by the nucleic acid construct according to any one of claims 1 to 18.
22. A transgenic non-human animal according to claim 21, in which the non-human animal is a mammal.
23. A transgenic non-human mammal according to claim 22, in which the mammal is a mouse.
24. A transgenic non-human animal according to any one of claims 21 to 23 wherein the secreted/excreted reporter product or protein or molecule is excreted in a body fluid selected from the group comprising urine, saliva, tears, milk, cerebrospinal fluid and semen.
25. A transgenic non-human animal according to any one of claims 21 to 24 wherein the secreted/excreted reporter product or protein or molecule is excreted in urine.
26. A host cell according to claim 19 or cell line according to claim 20 or a transgenic non-human animal according to any one of claims 21 to 25 wherein the secreted/excreted reporter moiety is of relatively low molecular weight, in the region of < 60-120kDa.
27. A host cell according to claim 19 or a cell line according to claim 20 or a transgenic non-human animal according to any one of claims 21 to 25 wherein the secreted/excreted reporter moiety possesses a hydrophilic globular tertiary structure,

has low bio-activity is and is clearly distinguishable from native molecules so that it is readily detectable and quantifiable.

28. A host cell according to claim 19 or a cell line according to claim 20 or a transgenic non-human animal according to any one of claims 21 to 25 comprising more than one nucleic acid construct according to claims 1 to 18.

29. Use of a nucleic acid construct according to any one of claims 1 to 18 for the detection of a gene activation event resulting from a change in altered metabolic status in a cell *in vitro* or *in vivo*.

30. Use according to claim 29, in which the gene activation event is the induction of toxicological stress, metabolic changes, or viral, bacterial, fungal or parasitic infection.

31. A method of detecting a gene activation event in a cell *in vitro* or *in vivo*, comprising assaying a host cell stably transfected with a nucleic acid construct in accordance with any one of claims 1 to 18, or a transgenic non-human animal according to any one of claims 21 to 25, in which the cell or animal is subjected to a gene activation event that is signalled by expression of a secreted/excreted reporter protein optionally the protein being tagged with an epitope.

32. A method of screening for, or monitoring of, toxicologically induced stress in a cell or a cell line or a non-human animal, comprising the use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct according to any one of claims 1 to 18.

33. A method for screening and characterising viral, bacterial, fungal, and parasitic infection or for screening for cancer, inflammatory disease, cardiovascular disease, metabolic disease, neurological disease and disease with a genetic basis comprising the

use of a cell, cell line or non human animal which has been transfected with or carries a nucleic acid construct according to any one of claims 1 to 18.